C1 Cont.

encoded by a polynucleotide comprising SEQ ID NO: 307 or a complement of said sequence.

C2

60. (Twice amended) A diagnostic kit, comprising:

(a) a polynucleotide according to claim 4; and

(b) a detection reagent for use in a polymerase chain reaction hybridization assay.



REMARKS

Claims 4-6, 16 and 60 are presently being examined on the merits. Claims 4, 5 and 60 have been amended. Certain pending claims have been amended to expedite prosecution on certain embodiments of the invention. It is urged that support for all the above amendments may be found throughout the specification as originally filed (see for example pages 91 and 98) and that none of the amendments constitute new matter. It should also be noted that the above amendments are not to be construed as acquiescence with regard to the Office's rejections. Applicants reserve the right to pursue any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application.

***Rejection of Claims 4-5 and 60 Under 35 U.S.C. § 112, second paragraph***

Claims 4-5 and 60 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

The Office indicates that claims 4 and 60 are indefinite because it is not clear as to what 15 amino acids can be considered as residues of a breast tumor protein. Claims 4-5 and 60 are considered indefinite over "the tumor protein" due to lack of antecedent basis. And finally claim 60 is considered indefinite over the use of "a diagnostic reagent".

Applicants respectfully traverse these grounds for rejection. As discussed above, claims 4, 5 and 60 have been amended merely to expedite prosecution on certain

embodiments of the invention. Claim 4 now reads in part "at least 15 contiguous amino acid residues of a breast tumor protein, wherein the breast tumor protein". Claim 5 now reads, in part, "the breast tumor protein" and claims 60 reads, in part, "a detection reagent." Support for the amendments can be found throughout the specification as filed, see in particular, pages 91 and 98.

Applicants respectfully submit that the above amendments and comments obviate and overcome the rejection and kindly request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

***Rejection of Claims 4 and 60 Under 35 U.S.C. § 112, first paragraph***

Claims 4 and 60 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Office indicates that the specification does not provide adequate written description for "an isolated polynucleotide [of SEQ ID NO:307] encoding at least 15 amino acid residues of breast tumor protein."

Applicants respectfully traverse this ground for rejection. However, as discussed above, merely to advance the claims toward allowance, and without acquiescing, claims 4 and 60 have been amended to recite in part "at least 15 contiguous amino acid residues of a breast tumor protein."

Applicants respectfully submit that the above amendments and comments obviate and overcome the rejection and kindly request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

***Rejection of Claims 4-6, 16 and 60 Under 35 U.S.C. § 101***

Claims 4-6, 16 and 60 are rejected under 35 U.S.C. § 101 and 112, first paragraph, because the Office alleges that the claimed invention lacks patentable utility due to its not being supported by specific, substantial, and credible utility or, in the alternative, a well-established utility.

Applicants respectfully traverse this ground for rejection. The pending claims are drawn to polynucleotides encoding at least 15 contiguous amino acid residues of a breast tumor protein, wherein the breast tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising SEQ ID NO: 307 or a complement of said sequence. As discussed in Example 1 of the specification (page 103, lines 8 – 24), these sequences were identified using a differential display PCR technique specifically designed to isolate sequences specific to breast tumor tissue. The specification clearly states that these sequences were isolated from bands that were observed to be specific to RNA fingerprint patterns of breast tumor tissue. It is thus urged that the claimed polypeptides may be successfully employed to detect the presence of breast cancer in a biological sample. Methods for employing the claimed polypeptides to diagnose breast cancer are clearly taught in the specification at pages 91-99. Applicants thus submit that one of skill in the art to which the present invention pertains, on being provided with the instant specification, would clearly be able to use the claimed polynucleotides to detect the presence of breast cancer

Applicants respectfully submit that the above amendments and comments obviate and overcome the rejection and request reconsideration and withdrawal of the rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph.

***Rejection of Claims 4 and 60 Under U.S.C. § 102(b)***

Claims 4 and 60 are rejected under 35 U.S.C. § 102 (b), as being anticipated by Bedin et al. (Geneseq Accession No. AAT96475, February 28th, 1998).

The Office believes that Geneseq Accession No. AAT96475 encodes at least 15 amino acid residues of a breast tumor protein wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide comprising SEQ ID NO: 307. The Office offers search result #11 in support of its claim.

Applicants respectfully traverse this ground for rejection. To qualify under 35 U.S.C. § 102 (b), the reference must teach each and every element of the claimed invention, in addition to being previously patented or described in a printed publication anywhere in the world, or in public use or on sale in the US, more than one year before

the date Applicant applied for a patent. In this case, the Bedin et al. disclosure fails to teach each and every element of the claimed in invention. The Office has provided search result #11 which contains an alignment of the polynucleotide sequences of SEQ ID NO: 301 and AAT96475. The search results indicates that there is 81% best local similarity. It is easy to see from the search result that there are very few regions of complete homology between the two sequences. There are numerous base pair deletions and insertions when compared to the polynucleotide sequence of SEQ ID NO:307, including a 70 bp insertion in the AAT96475 sequence disclosed in search result #11. The polynucleotide sequence disclosed in AAT96475 does not disclose SEQ ID NO:307.

On page 103 of Applicants' specification, at lines 23-24, is provided "The full-length sequence [of B311D] is provided in SEQ ID NO:307, with the corresponding amino acid sequence being provided in SEQ ID NO:308." The region corresponding to translated amino sequence of SEQ ID NO: 308 can be found beginning at bp 407 and ending at bp 712 of SEQ ID NO: 307. This region corresponds to the region between bp 1321 to bp 1628 of the AAT96475 sequence as presented in search result #11. The Applicants wish to direct the Office's attention, in particular, to bps 1231-1323 of the AAT96475 sequence, where one of the numerous base pair changes occurs between these sequences. SEQ ID NO: 307 has the sequence "atg" encoding a methionine residue, the start of the polypeptide described in SEQ ID NO: 308. The AAT96475 sequence has the sequence "gtg" which does not encode a methionine residue. Geneseq record AAT96475 does not indicate a coding region nor a corresponding polypeptide sequence that Bedin et al. contemplate arising from the disclosed polynucleotide sequence.

Bedin et al. indicate that AAT96475 is derived from the multiple sclerosis related virus 1 (MSRV-1), associated with multiple sclerosis and some association with rheumatoid arthritis. Bedin et al. indicates that the nucleic acids can be used in the diagnosis of multiple sclerosis and rheumatoid arthritis. This disclosure does not teach or suggest breast tumor proteins.

Applicants' invention, as claimed, requires "An isolated polynucleotide encoding at least 15 contiguous amino acid residues of a breast tumor protein, wherein the breast tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising SEQ ID NO: 307 or a complement of said sequence." The polynucleotide

sequence disclosed in AAT96475 does not comprise the polynucleotide of SEQ ID NO: 307 and lacks the codon sequence of the starting methionine residue of SEQ ID NO:308 which would identify the frame (of the 6 possible frames) in which the polypeptide sequence must be read. The sequence described by Bedin et al. is not identified as a polynucleotide that encodes a breast tumor antigen, the association is made to multiple sclerosis. The Office therefore has not met the requirements of § 102(b) as the disclosure of Bedin et al. does not teach each and every element of Applicants' claimed invention.

Applicants respectfully submit that the above amendments and comments obviate and overcome the rejection and request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

***Rejection of Claim 60 Under 35 U.S.C. § 103(a)***

Claim 60 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Bedin et al. (Geneseq Accession No. AAT96475, February 28th, 1998) as applied to claim 4 and in further in view of Stratagene Catalog (1998).

The Office believes that Bedin et al. teach Applicants' invention as described in claim 4 and when combined with reagent kits for performing DNA assays described in the Stratagene Catalog, renders the Applicants' invention obvious.

Applicants' respectfully traverse this ground for rejection. The Office has the burden of setting forth a *prima facie* case of obviousness. As discussed above, Bedin et al. do not teach or suggest Applicants' claimed invention as set out in claims 4 and 60. The combination with the Stratagene Catalog does not correct the defects of the Bedin et al. The Office provides a single page from the catalogue as support for its assertion. This page, titled "Gene Characterization Kits" merely provides advertising rationale for choosing one of the offered "gene characterization kits" over purchasing all the components separately. The table of contents directs the reader to other pages where DNA and RNA sequencing kits, RNA transcription and mRNA capping kits can be found. The table of contents also directs the reader to pages containing exo/mung nuclease detection, in vitro express translation and picoBlue immunoscreening kits. The Stratagene catalog does not teach or suggest the polynucleotides of claim 4, nor does the catalog teach or suggest a PCR or hybridization-based kit to detect the polynucleotides of claim 4. Since neither the Bedin et al. reference nor the Stratagene Catalog,

independently or in combination teach or suggest Applicants' invention as claimed in claim 60. As such, the Office has failed to present a *prima facie* case of obviousness and the rejection should be withdrawn.

Applicants respectfully submit that the above amendments and comments obviate and overcome the rejection and request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

The Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version With Markings to Show Changes Made.**"

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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## VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 4, 5, and 60 have been amended as follows:

4. (Twice Amended) An isolated polynucleotide encoding at least 15 contiguous amino acid residues of a breast tumor protein, wherein the breast tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising SEQ ID NO: 307 or a complement of said sequence.

5. (Twice Amended) An isolated polynucleotide encoding a breast tumor protein, wherein the breast tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising SEQ ID NO: 307 or a complement of said sequence.

60. (Twice amended) A diagnostic kit, comprising:

(a) a polynucleotide according to claim 4; and

(b) a ~~diagnostic~~ detection reagent for use in a polymerase chain reaction or hybridization assay.